REMARKS

In view of the comments which follow, and pursuant to 37 CFR §1.111, reconsideration of the official action dated July 23, 2002 is respectfully requested by Applicants.

In response to Applicants' previous amendment, the Examiner has withdrawn all previous rejections under 35 USC §112, second paragraph, as well as the objection to claims 30-33. However, the Examiner has cited new 35 USC §103 (a) rejections, thereby rendering Applicants' previous arguments moot. In addition to the Talley, Haugland and Stratagene references previously cited, the Examiner has now cited the Carrico reference.

Rejection 1 under 35 USC §103 (a)

Claims 30-31 have been rejected under 35 USC §103 (a) as being unpatentable over U.S. Patent 6,132,955 issued October 17, 2000 to Talley *et al.* (hereinafter "Talley") in view of U.S. Patent 5,798,276 issued August 25, 1998 to Haugland *et al.* (hereinafter "Haugland") and further in view of U.S. Patent 4,743,535 issued May 10, 1988 to Carrico (hereinafter "Carrico").

The Examiner argues that Talley teaches a method for quantitative electrochemiluminescence detection of an oligonucleotide target analyte in a sample, the method comprising the steps of:

1. preparing an assay mixture comprising the sample, one or more assay reagents comprising a labeled complex comprising an ECL label selected from ruthenium bipyridine complexes and osmium bipyridine complexes attached to an oligonucleotide probe complementary to the analyte and capable of hybridizing therewith, the label capable of generating a detectable ECL emission, wherein the labeled complex is immobilized on a magnetic particle, and a coreactant,

2. bringing the assay mixture into contact with a working electrode,

3. applying a potential to the electrode, thereby enabling an ECL reaction to proceed,

4. separating unhybridized labeled complex from hybridized complex,

5. measuring the ECL emission produced by the label hybridized to the analyte via the oligonucleotide probe, and

6. correlating the measured ECL emission with the amount of the analyte in the sample.

The Examiner states that Talley does not teach a method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone.

Haugland, the Examiner argues, teaches a method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone.

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to include the group of chemicals containing phenol of Haugland in the method of Talley, since Haugland states "Dyes that are able to preferentially bind to a specific biological ingredient in a sample enable the researcher to determine the presence or quantity of that specific ingredient. In addition, specific cellular structures can be monitored with respect to their spatial and temporal distribution in diverse environments. Many applications utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or systhetic polymers to make fluorescent conjugates." The Examiner argues that an ordinary practitioner would have been motivated to combine and compare "the electrochemiluminescence quenching chemicals

containing deferentially substituted phenol ring of Haugland" (emphasis added by Applicants) into the method of Talley in order to achieve the express advantages, as noted by Haugland, of dyes that are able to preferentially bind to a specific biological ingredient in a sample, which enables the researcher to determine the presence or quantity of that specific ingredient and in addition, to monitor specific cellular structures with respect to their spatial and temporal distribution in diverse environments and in addition has many applications that utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates.

The Examiner states that Talley in view of Haugland do not teach the combination of dyes containing ECL quenching moiety and ECL inducing moiety.

The Examiner argues that Carrico teaches the combination of dyes containing ECL quenching moiety and ECL inducing moiety (Column 2, lines 34-54).

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the combination of dyes containing ECL quenching moiety and ECL inducing moiety of Carrico in the method of Haugland in view of Talley since Carrico states, "It is proposed to employ a pair of probes which hybridize to contiguous regions on a polynucleotide sequence of interest and to label one probe with a chemiluminescent catalyst such as the enzyme peroxidase and the other with an absorber molecule for the chemiluminescent emission. The catalyst and absorber labels must be situated near the contiguous terminal ends of the respective probes such that upon hybridization there is observed quenching of the chemiluminescent emission by energy transfer to the absorber molecule (emphasis added by Applicants)." The Examiner argues that an ordinary practitioner would have been motivated to combine and substitute the combination of dyes containing ECL quenching moiety and ECL inducing moiety of Carrico in the

method of Haugland in view of Talley in order to achieve the express advantages, as noted by Carrico, of a method which provides probes such that upon hybridization there is observed quenching of the chemiluminescent emission by energy transfer to the absorber molecule.

Applicants argue that the Examiner's case for *prima facie* obviousness has not been made. In making his argument, the Examiner has mischaracterized the fluorescent dye compounds of Haugland as "electrochemiluminescence quenching chemicals containing deferentially substituted phenol ring". Haugland's dyes are neither "electrochemiluminescent" nor "quenching" nor "containing phenol". The Examiner argues that one having ordinary skill in the art would want to include the "group of chemicals containing phenol of Haugland" in the method of Talley. Applicants point out that Haugland does not teach an ECL quenching moiety. Haugland teaches reactive fluorescent dyes that react with substances having reactive functional groups which can include phenol. Among the advantages of Hauglands derivatives are "selective reactivity with a broader range of functional groups" (column 2, lines 54-55). Haugland teaches that selected embodiments of the invention, i.e., the novel fluorescent dyes, "react with, and form conjugates with, substances having reactive functional groups, including amines, thiols, alcohols and phenols" (column 2, lines 64-67). Thus, Haugland does not teach a reagent comprising at least one moiety selected from the group consisting of phenol and benzoquinone, but rather, Haugland teaches a reagent that is reactive with a reactive phenol group. Furthermore, a person skilled in the art would have no reason to try to combine a fluorescent dye of Haugland with the electrochemiluminescent method of Talley. Finally, Applicants argue that it is reasonable to expect that the combination of Talley and Haugland would either be inoperable or lack utility as an electrochemiluminescent assay, with which Talley (and the present invention) are concerned.

The addition of the Carrico reference to those of Talley and Haugland still does not produce the present invention. Carrico describes nucleic acid hybridization assays and the problem of the necessity of a separate step for separation of hybridized and unhybridized probes. The specific teaching relied upon by the Examiner (column 2, lines 34-54) describes a chemiluminescent catalyst such as the enzyme peroxidase, and an absorber molecule for the chemiluminescent emission. Applicants point out, first of all, that a "chemiluminescent catalyst such as the enzyme peroxidase" is not anything like "an electrochemiluminescent label selected from the group consisting of ruthenium bipyridine complexes and osmium bipyridine complexes" as required by Applicants invention, and a person skilled in the art would have no reason to try to combine "an absorber molecule for chemiluminescent emission" in an assay in which an "electrochemiluminescent label" is used. As the Examiner admits, Talley in view of Haugland does not teach the combination of an electrochemiluminescent label and an electrochemiluminescent quenching moiety. Carrico does not teach this combination either, nor does the combination of Talley, Haugland and Carrico teach or suggest an electrochemiluminescent label and an electrochemiluminescent quenching moiety.

Applicants argue that the combination of the Talley, Haugland and Carrico references does not make the claimed invention and that the Examiner's case of *prima facie* obviousness has not been made. None of the references, either singly or combined, teaches or suggests the use of an electrochemiluminescent quencher in an electrochemiluminescence assay for an oligonucleotide analyte. The Examiner's reconsideration of the rejection of claims 30-31 under 35 USC §103 (a) in light of the above remarks is respectfully requested by Applicants.

Rejection 2 under 35 USC §103 (a)

Claims 30-33 have been rejected under 35 USC §103 (a) as being unpatentable over Talley in view of Haugland further in view of Carrico and further in view of Stratagene Catalog (1988, page 39, hereinafter "Stratagene").

The Examiner argues that Talley in view of Haugland and further in view of Carrico expressly teaches the method claims and assay reagents of claims 30-31, as described in Examiner's argument above. Talley in view of Haugland and further in view of Carrico does not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit. Stratagene teaches a motivation to combine reagents into kit format.

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, ECL label and ECL quenching moiety of Talley in view of Haugland and further in view of Carrico into a kit format as discussed by Stratagene since Stratagene teaches a motivation for combining reagents for use in an assay into a kit.

Applicants argue that even the combination of all four references still do not make the claimed invention and that the Examiner's case of *prima facie* obviousness has not been made. None of the reference, either singly or combined, teaches or suggests the use of an electrochemiluminescent quencher in an electrochemiluminescence assay for an oligonucleotide analyte. The examiner's reconsideration of the rejection of claims 30-33 under 35 USC §103 (a) in light of the above remarks is respectfully requested by Applicants.

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Applicants submit that their application is now in condition for allowance, and favorable reconsideration of their application in light of the above remarks is respectfully requested. Allowance of claims 30-33 at an early date is earnestly solicited.

The Examiner is hereby authorized to charge any fees associated with this amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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